TRANSLATION

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
HT0418		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2004/017497	25.11.2004	26.02.2004

International Patent Classification (IPC) or national classification and IPC

C12N15/09(2006.01), A61K48/00(2006.01), A61P29/00(2006.01), C12Q1/68(2006.01)

Applicant

SHIOZAWA, Shunichi

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))
      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

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International application No.
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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

nos. _____ as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* _____ received by this Authority on _____

nos.* _____ received by this Authority on _____

☐ the drawings:

sheets _____ as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

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Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-12	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-12	NO
Industrial applicability (IA)	Claims	1-12	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Document 1: Dai 26 Kai The Molecular Biology Society of Japan Nenkai Program - Koen Yoshishu (pub. 25 November 2003), page 1035, 4PC-113

Document 2: WO 02/34912 A1 (The Industry Research Organization), 02 May 2002 & EP 1335021 A1 & US 2004/0013655 A1

Document 3: WO 01/32921 A2 (Shunichi SHIOZAWA), 10 May 2001 & AU 200110530 A & KR 2002065498 A

Claims 1 to 12

The inventions set forth in claims 1 to 12 do not involve an inventive step in the light of documents 1 to 3 cited in the international search report.

With regards to document 1, however, the applicant has made a declaration as to non-prejudicial disclosures or exceptions to lack of novelty.

As a result of a methylation analysis of the promoter region for the death receptor 3 gene (the DR3 gene), which is one of the genes associated with rheumatoid arthritis (RA), document 1 confirms that allele-specific methylation occurred in the CpG region that is present approximately 380 to 180 bp upstream from

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

the ATG site, and that the alleles of the CpG region downstream from the ATG site did not undergo methylation. Furthermore, document 1 also confirms that the methylation of this region affected the transcription of the DR3 gene, thus suggesting that the region in question is associated with the onset of RA.

Meanwhile, documents 2 and 3 disclose the structural gene within the death receptor 3 gene (the DR3 gene), which is one of the genes associated with rheumatoid arthritis (RA), and also disclose a portion of the base sequence on the upstream side thereof; therein, said documents indicate that it is possible to diagnose RA and determine the possibility of the onset thereof by detecting for said base sequence. In addition, document 2 also discloses a method and a medicament for the treatment of rheumatoid arthritis which employ said base sequence.

In the light of the disclosures in document 1, it would have been easy for a person skilled in the art to conceive of determining the base sequence of the promoter region for the DR3 gene disclosed in documents 2 and 3 so that it would then be possible to diagnose RA and determine the possibility of the onset thereof by detecting for said base sequence, and so that it would also be possible to treat rheumatoid arthritis by means of methods and/or medicaments that employ said base sequence.

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

(1)

With regards to the medicaments set forth in claims 11 and 12, the description does not set forth the base sequence of the specific polynucleotide that is used for the treatment, and does not present any test results from pharmacological tests or the like.

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☐ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☒ contained in the international application as filed

   ☐ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment* on _____

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*